DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/31/08 has been entered.

2. Applicant's election without traverse of Group II (claims 13-23) in the reply filed on 7/17/06 is reiterated. Claims 13 and 14 have been modified. New claim 27 has been added. Claims 1-12, 15-19 and 22-23 have been canceled without prejudice or disclaimer. Currently claims 13-14, 20-21, and 24-27 are pending and under consideration.

3. Rejections and/or objections of record not restated herein have been withdrawn.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 13 and 27 as well as dependent claims 14, 20-21 and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 13 is directed to a method for reducing the risk of mortality in a subject. The method steps (a, i-iii) merely provides a pathogen, a subject having said pathogen, and an anti-vimentin antibody. In claim 13 step iii, the anti-vimentin antibody is administered to the subject. However, the relationship of the pathogen of *step i* and the remaining procedures of the method are ambiguous. Therefore, it is not clear that the pathogen is administer to the subject. This makes that claims vague and indefinite. It is not clear if the pathogen in present within the subject prior to antibody administration, if Applicant intends to administer a pathogen to the subject, or if the pathogen is apart of the claimed method. It is suggested that the relationship of the pathogen in the claimed method be clearly set forth in order to obviate this rejection. In other words the claims should clearly recite that the *"pathogen is administered to the subject"*. Appropriate correction is required.

B. Claim 27 is vague and indefinite in reciting that the pathogen has sepsis. It is not clear if it's Applicant intent to mean the subject has sepsis. As recited the metes and bounds of the claim can not be determined. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 13-14, 20-21, and 24-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing mortality in vimentin knockout mice via the administration of anti-vimentin antibodies 15 min prior to an *E. coli* (J-96) intraperitoneal injection (see examples 6 and 7 on pages 78-79), it does not reasonably provide enablement for any and all methods for reducing mortality in any and all subjects having any pathogen/sepsis via the administration of any and all anti vimentin antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets enablement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988).

Wands states on page 1404,

"Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims."

Specifically the claims are drawn to a method of administering an anti-vimentin antibody to any and all subjects to treat any bacterial pathogen causing any and all sepsis. This reads on *in vivo* vaccine procedures and the disclosure does not have support for this type of protocol. The specification teaches that anti-vimentin IgG antibodies may have a phagocytic and killing activity on MDM cells cultured *in vitro*. See page 72 lines 13-24 and example 4 on page 77, for example. The specification also exemplifies reduced *E.coli* septicemia and mortality. However, this reduction appears to *only* be seen if vimentin knockout mice are administered anti-vimentin antibodies - 15 minutes prior to an *E. coli* (J-96) intraperitoneal injection (see examples 6 and 7 on pages 78-79). These teachings do not enable one skilled in the art to effectively practice a method for reducing mortality in any subject as set forth in the instant claims.

The prior art teaches that the presence of anti vimentin antibodies is linked to detrimental results in patients. See the abstract to Danskine et al. (Human Immunology, 2002, Vol.63, Supplement 1, pp S30) wherein anti-vimentin antibodies were correlated with acute and chronic cardiac transplantation rejection. Also see the reference to Yang et al. (Clinical and Experimental Immunology, April 2002, Vol.128, No.1, pp 169-174) were high levels of antivimentin antibodies are linked to IPF (idiopathic pulmonary fibrosis), NSIP (non-specific interstitial pneumonia), systemic lupus erythematosus, progressive systemic sclerosis and RA. Thus from the prior art teaching the administration of anti-vimentin antibodies to a subject would appear to induce diseases and/or disorders linked to bacterial pathogens. This is contrary to the instant invention which is directed to reduced risk of mortality. See abstract and page 128 – Discussion.

Further, the specification does not set forth any *in vivo* data showing the protective ability of anti-vimentin antibody administration to a subject other than vimentin knock out mice with goat anti-vimentin serum. Example 7 on page 79 teaches that "mice receiving goat anti-vimentin show a 38% reduction in mortality compared to those receiving *anti-vimentin antibody* free serum (figure 9)". However, this is only exemplified in 13 week old mice with lethal dosages of *E. coli* (J-96) wherein the mice were injected with goat anti-vimentin serum 15 min prior to *E. coli* (J-96) injection. These particulars are not recited in the instant claims. Therefore the broad claim of killing any and all bacterial pathogens, in any and all subjects, with any and all anti-vimentin antibodies is not enabled. The prior art teaches that species specific antibodies against vimentin have different reactivity. See abstract to Bohn et al. (Experimental Cell Research, Vol.201, No.1, July 1992, pages 1-7). The art also teaches that in vitro results can not predict in vivo antibody responses. See Pallini et al. (Journal of Neuro-Oncology, Vol. 49, 2000, pages 9-17). As such the reduction of mortality in any and all subjects having any pathogen/sepsis via the administration of any and all anti vimentin antibodies, is not apparent and would require undue experimentation.

Devoid of results supporting in vivo killing of a other pathogen/sepsis by other species of anti-vimentin antibodies, the skilled artisan would not be able to predict the outcome of the administration of the claimed anti-vimentin antibodies activity, i.e. would not be able to accurately predict if anti-vimentin antibodies agents would be useful in the claimed purpose.

The agents/drug/antibody/vaccine (having anti-vimentin antibody activity) art is highly unpredictable and the instant specification fails to provide any information that any one of the recited conjugates would provide immunity to a human from a bacterial pathogen. There are no immunological experiments provided to demonstrate that the claimed proteins or fragments are capable of mounting an efficient immune response and, more importantly, there are no challenge experiments to demonstrate that a person immunized with any one of the claimed anti-vimentin antibodies would be protected. There are no protocols provided which demonstrate which anti-*vimentin antibody* agents would be effective in immunization, nor are there any protocols detailing the amount of protein which is needed to mount a sufficient immune response.

There is no teaching as to what would be the other effective routes of administration for the claimed agents/drug/antibody/vaccine (other than IP in mice). There is merely a general outline of agents/drug/antibody/vaccine and their administration, which does not directly apply to the instant invention. It is unclear that one of skill in the art could follow these general guidelines and achieve immunization (protection/treatment) of a human against all pathogens/sepsis without undue experimentation.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from *in vitro* antibody reactivity studies is problematic. Unfortunately, the art is replete with instances where even well characterized antigens that induce an *in vitro* neutralizing antibody response fail to elicit *in vivo* protective immunity. See Blasi et al. (Clinical Pulmonary Medicine, 2002, 9/1, 6-12 -Abstract) wherein *in vitro* data regarding *C. pneumonia* activity/treatment could not predict optimal dosing and length for in vivo activity/treatment.

Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful anti-*vimentin antibody* agent with out prior demonstration of efficacy in the particular diseases.

Specifically, anti-*vimentin antibodies* do not necessarily end up providing any protective immunoprotection and have actually been linked to various disease states. Yang et al. (Clinical and Experimental Immunology, April 2002, Vol.128, No.1, pp 169-174)

It has been set forth above that 1) the experimentation required to generate an agent/drug/antibody/vaccine which provides treatment in a mammal/human against *a pathogen* would be great as 2) there are no immunological experiments provided to demonstrate that the claimed agents are capable of mounting an efficient immune response and, more importantly, there are no challenge experiments to demonstrate that a person immunized with any one of the claimed anti-vimentin antibody agents would be protected from *a pathogen.*

There are no protocols provided which demonstrate which proteins or portions of the proteins would be effective in immunization, nor are there any protocols detailing the amount of protein which is needed to mount a sufficient immune response, 3) there are not working examples provided in the instant specification, 4) the nature of the invention is a method for producing an anti-vimentin antibody agents which would provide complete protection in a host against *a pathogen/sepsis*, 5) the relevant skill of those in the art is high yet 6) the state of the prior art has been shown to be highly unpredictable as evidenced by the cited references and lastly 7) the claims broadly encompass agents which would provide protection in humans to any *pathogen/sepsis*.

There is insufficient evidence or nexus that would lead the skilled artisan to predict reducing mortality in any and all subjects having any pathogen/sepsis via the administration of any and all anti vimentin antibodies. In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which are reasonably predictive, commensurate in scope with the claimed invention, and in view of the teachings of In re Wands, 8 USPQ2d 1400; it has been determined that the level of experimentation required to enable the scope/breadth of the instant claims is undue.

Response to Arguments

Applicant arguments and amendments against the Enablement rejection of record was found persuasive. Accordingly the claims and disclosure were reconsidered. However, A Scope of Enablement rejection has been set forth.

6. For reasons aforementioned, no claims are allowed.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300.

In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA or CANADA) or 571-272-1000.

Lisa V. Cook
Remsen 3C-59
(571) 272-0816
4/9/08

/Lisa V. Cook/
Primary Examiner, Art Unit 1641